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CHALKER FLORES, LLP			STEELE, AMBER D	
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Suite 1036			PAPER NUMBER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/828,934

Applicant(s)

GORENSTEIN ET AL.

Examiner

Amber D. Steele

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 June 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-78 is/are pending in the application.
- 4a) Of the above claim(s) 12-77 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-11 and 78 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 21 April 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Claims

1. The amendment to the claims received on October 4, 2006 amended claim 7.

The amendment to the claims received on June 25, 2007 amended claim 7 and added new claim 78.

Claims 1-78 are currently pending.

Claims 1-11 and 78 are currently under consideration.

Election/Restrictions

2. Applicant's elected Group I (claims 1-11 and new claim 78) without traverse in the reply filed on October 4, 2006.

3. Claims 12-77 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim.

Election was made **without** traverse in the reply filed on October 4, 2006.

4. This application contains claims 12-77 drawn to an invention nonelected without traverse in the reply filed on October 4, 2006. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01. Please note: applicants have not amended claims 42-77 and thus may lose the right to rejoinder (please refer to the rejoinder section below).

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Rejoinder

5. Restriction between product and process claims was required. The applicant elected claims directed to a product. If a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. Process claims that depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all the criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained.

Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. Failure to do so may result in a loss of the right to a rejoinder. Further, note that the prohibition against double

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patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Priority

6. Applicants state that the present application is a CIP of U.S. application 10/272,509 filed October 16, 2002 which is a CIP of U.S. application 09/425,798 filed October 25, 1999 (now U.S. Patent 6,423,493) which is a CIP of U.S. application 09/425,804 filed October 25, 1999 (now U.S. Patent 6,867,289) which claims benefit of U.S. provisional application 60/105,600 filed October 26, 1998.

7. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed applications, Application Nos. 10/272,509; 09/425,798; 09/425,804; and 60/105,600, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. U.S. Application Nos. 10/272,509; 09/425,798; 09/425,804; and 60/105,600 do not disclose thio-

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modified aptamers that bind TGF- β including SEQ ID NO: 62. Thus, the filing date (April 21, 2004) of the present application is the priority date for the presently claimed invention.

Information Disclosure Statement

8. The reference (WO 00/47774) filed June 25, 2007 fails to comply with 37 CFR 1.98(a)(1), which requires the following: (1) a list of all patents, publications, applications, or other information submitted for consideration by the Office; (2) U.S. patents and U.S. patent application publications listed in a section separately from citations of other documents; (3) the application number of the application in which the information disclosure statement is being submitted on each page of the list; (4) a column that provides a blank space next to each document to be considered, for the examiner's initials; and (5) a heading that clearly indicates that the list is an information disclosure statement. The reference has been placed in the application file, but the reference has not been considered.

Invention as Claimed

9. A partially thio-modified aptamer that binds to a TGF- β protein and variations thereof.

Withdrawn Objections

10. The objection to the disclosure regarding the embedded hyperlinks is withdrawn in view of the amendments to the specification received on June 25, 2007.

11. The objection to the disclosure regarding the lack of priority information in the first line of the specification is withdrawn in view of the amendments to the specification received on June 25, 2007.

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12. The objections to claim 7 are withdrawn in view of the claim amendments received on June 25, 2007.

New Rejections Necessitated by Amendment

Claim Rejections - 35 USC § 112

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claim 7 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. One of skill in the art would not be able to determine the scope of the presently claimed invention. Claim 7 reads "wherein the aptamer comprises the sequence and modifications of SEQ ID NO: 62". In the sequence listing received on October 8, 2004, SEQ ID NO: 62 is identified as the following:

Section 210: 62 (i.e. SEQ ID NO:)

Section 211: 74 (i.e. sequence length)

Section 212: DNA (i.e. sequence type)

Section 213: Artificial Sequence (i.e. organism sequence is from)

Section 220: blank (i.e. features including modifications)

Section 223: Description of Artificial Sequence: Synthetic oligonucleotide (i.e. other information including modifications)

Section 400: cagtccggat gctctagagt gacgtgaaag tgcaatggat ccaggacccc acacgaatct cgtgaagccg agcg (i.e. sequence)

Thus, SEQ ID NO: 62 does not have any modifications. For example, would modifications of SEQ ID NO: 62 include sequences with 10%, 20%, 40%, 80%, etc. complementary/identity; would the addition of a thiol to SEQ ID NO: 62 be a modification; would the removal of the thio-modification required by independent claim 1 be considered the modification in claim 7,

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would the addition of other chemical compounds, nucleic acids, amino acids, etc. be considered modifications; etc.?

15. Claim 78 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. One of skill in the art would not be able to determine the scope of the presently claimed invention. Claim 78 reads “[a] partially thio-modified aptamer that binds to TGF- β comprising a sequence and modifications that is at least 80% complementary to SEQ ID NO: 62”. For example, would modifications of SEQ ID NO: 62 include mutations that maintain 80% complementarity/identity; would the addition of a thiol to SEQ ID NO: 62 be a modification; would the addition of other chemical compounds, nucleic acids, amino acids, etc. be considered modifications; etc.?

Maintained Rejections

16. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Please note: the rejections may have been altered to reflect the claim amendments received on June 25, 2007.

Claim Rejections - 35 USC § 102

17. Claims 1-6 and 8-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Pagratis et al. U.S. Patent 6,346,611 issued February 12, 2002.

For present claims 1-6 and 8-11, Pagratis et al. teach aptamers that bind human TGF β 1, TGF β 2, and TGF β 2 dimers wherein the aptamers may comprise a labeling tag, phosphorothioate modifications, and/or be diluted in saline (i.e. pharmaceutically acceptable salts and diluent;

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please refer to the entire specification particularly the abstract; Figures; columns 1-2, 6-7, 10-13; Examples; Tables; claims 1-5). Regarding achiral aptamers, Pagratis et al. teaches various aptamers without providing the secondary structure for each therefore the symmetry of the structures cannot be readily determined. Please refer to MPEP § 2112.01 which states "Where the claimed and prior art products are identical or substantially identical in structure or composition anticipation or a *prima facie* case of obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990)".

Therefore, the presently claimed invention is anticipated by the teachings of Pagratis et al.

Arguments and Response

18. Applicants' arguments directed to the rejection under 35 USC 102 (b) as being anticipated by Pagratis et al. for claims 1-6 and 8-11 were considered but are not persuasive for the following reasons.

Applicants contend that Pagratis et al. is non-enabling and does not teach partial thio-modification. In addition, applicants reference commonly assigned U.S. Patent 6,867,289.

Applicants' arguments are not convincing since the teachings of Pagratis et al. anticipate the aptamers of the instant claims. Pagratis et al. teach phosphorothioate modifications including 5' and 3' capping (i.e. partial thio-modification; please refer to the entire specification

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particularly column 13, lines 5-30). In response to applicants arguments that the prior art is non-enabling, applicants are respectfully directed to the following:

MPEP § 716.07 which states that every patent is presumed valid (35 U.S.C. 282) and that presumption includes the presumption of operability (see *Metropolitan Eng. Co. v. Coe*, 78 F.2d 199 25 USPQ 216 (D.C. Cir. 1935)).

MPEP § 2121 which reads “[w]hen the reference relied on expressly anticipates or makes obvious all of the elements of the claimed invention, the reference is presumed to be operable...[o]nce such a reference is found, the burden is on applicant to provide facts rebutting the presumption of operability (see *In re Sasse*, 629 F.2d 675, 207 USPQ 107 (CCPA 1980)).

MPEP § 2145 which reads “[t]he arguments of counsel cannot take the place of evidence in the record (see *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965) and *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997)).

In addition, it is unclear to the examiner why applicants have referenced U.S. Patent 6,867,289 in the arguments. The priority claim to U.S. Patent 6,867,289 has been denied due to lack of disclosure of the presently claimed invention (please refer to section 7 above).

19. Claims 1-6 and 8-11 are rejected under 35 U.S.C. 102(e) as being anticipated by Pagratis et al. U.S. Patent 6,713,616 filed February 23, 2001.

For present claims 1-6 and 8-11, Pagratis et al. teach aptamers that bind to human TGFβ1, TGFβ2, and TGFβ2 dimers wherein the aptamers may comprise a labeling tag, phosphorothioate modifications, and/or be diluted in saline (i.e. pharmaceutically acceptable salts and diluent; please refer to entire specification particularly abstract; Figures; columns 1-2,

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4, 6-8, 10-14; Examples; Tables; claims 1-14). Regarding achiral aptamers, Pagratis et al. teaches various aptamers without providing the secondary structure for each therefore the symmetry of the structures cannot be readily determined. Please refer to MPEP § 2112.01 which states "Where the claimed and prior art products are identical or substantially identical in structure or composition anticipation or a *prima facie* case of obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990)".

Therefore, the presently claimed invention is anticipated by the teachings of Pagratis et al.

Arguments and Response

20. Applicants' arguments directed to the rejection under 35 USC 102 (e) as being anticipated by Pagratis et al. for claims 1-6 and 8-11 were considered but are not persuasive for the following reasons.

Applicants contend that Pagratis et al. is non-enabling and does not teach partial thio-modification. In addition, applicants reference commonly assigned U.S. Patent 6,867,289.

Applicants' arguments are not convincing since the teachings of Pagratis et al. anticipate the aptamers of the instant claims. Pagratis et al. teach phosphorothioate modifications including 5' and 3' capping (i.e. partial thio-modification; please refer to the entire specification particularly column 13, lines 16-33). In response to applicants arguments that the prior art is non-enabling, applicants are respectfully directed to the following:

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MPEP § 716.07 which states that every patent is presumed valid (35 U.S.C. 282) and that presumption includes the presumption of operability (see *Metropolitan Eng. Co. v. Coe*, 78 F.2d 199 25 USPQ 216 (D.C. Cir. 1935)).

MPEP § 2121 which reads “[w]hen the reference relied on expressly anticipates or makes obvious all of the elements of the claimed invention, the reference is presumed to be operable...[o]nce such a reference is found, the burden is on applicant to provide facts rebutting the presumption of operability (see *In re Sasse*, 629 F.2d 675, 207 USPQ 107 (CCPA 1980)).

MPEP § 2145 which reads “[t]he arguments of counsel cannot take the place of evidence in the record (see *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965) and *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997)).

In addition, it is unclear to the examiner why applicants have referenced U.S. Patent 6,867,289 in the arguments. The priority claim to U.S. Patent 6,867,289 has been denied due to lack of disclosure of the presently claimed invention (please refer to section 7 above).

21. Claims 1 and 7 are rejected under 35 U.S.C. 102(e) as being anticipated by Rubenfield et al. U.S. Patent 6,551,795 filed February 18, 1999.

For present claims 1 and 7, Rubenfield et al. teach thio-modified nucleic acids with less than 40% identity to present SEQ ID NO: 62 (please refer to the entire specification and SCORE results). Please refer to MPEP § 2112.01 which states “Where the claimed and prior art products are identical or substantially identical in structure or composition anticipation or a *prima facie* case of obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). “When the PTO shows a sound basis for believing that the products of the

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applicant and the prior art are the same, the applicant has the burden of showing that they are not.” *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990)”. For example,

Therefore, the presently claimed invention is anticipated by the teachings of Rubenfield et al.

Arguments and Response

22. Applicants’ arguments directed to the rejection under 35 USC 102 (e) as being anticipated by Rubenfield et al. for claims 1 and 7 were considered but are not persuasive for the following reasons.

Applicants contend that Rubenfield et al. do not teach partially thio-modified aptamers that are TGF- β specific and that Rubenfield et al. is not enabled.

Applicants’ arguments are not convincing since the teachings of Rubenfield et al. anticipate the modified sequence of SEQ ID NO: 62 of the instant claims. Rubenfield et al. teach a nucleic acid sequence with less than 40% identity to present SEQ ID NO: 62 wherein the modifications as stated in present claim 7 could include the removal of the thiol group(s) and mutations encompassing sequences with less than 40% identity to SEQ ID NO: 62 (please refer to the entire specification particularly sequence listing and SCORE results). In addition, Rubenfield et al. teach thio-modified proteins (please refer to paragraph 92).

In response to applicants arguments that the prior art is non-enabling, applicants are respectfully directed to the following:

MPEP § 716.07 which states that every patent is presumed valid (35 U.S.C. 282) and that presumption includes the presumption of operability (see *Metropolitan Eng. Co. v. Coë*, 78 F.2d 199 25 USPQ 216 (D.C. Cir. 1935)).

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MPEP § 2121 which reads “[w]hen the reference relied on expressly anticipates or makes obvious all of the elements of the claimed invention, the reference is presumed to be operable...[o]nce such a reference is found, the burden is on applicant to provide facts rebutting the presumption of operability (see *In re Sasse*, 629 F.2d 675, 207 USPQ 107 (CCPA 1980)).

MPEP § 2145 which reads “[t]he arguments of counsel cannot take the place of evidence in the record (see *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965) and *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997)).

Allowable Subject Matter

23. The exact sequence of SEQ ID NO: 62 was not found in the prior art. An independent claim drawn to a partially thio-modified aptamer comprising the nucleic acid of SEQ ID NO: 62 would be free of the prior art.

Conclusion

24. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

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however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Future Communications

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amber D. Steele whose telephone number is 571-272-5538. The examiner can normally be reached on Monday through Friday 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ADS

August 16, 2007



MARK L. SHIBUYA
PRIMARY EXAMINER